

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
in its capacity as elected Office

Date of mailing (day/month/year) 16 February 2001 (16.02.01)	
International application No. PCT/GB00/02364	Applicant's or agent's file reference ML/P32328
International filing date (day/month/year) 16 June 2000 (16.06.00)	Priority date (day/month/year) 16 June 1999 (16.06.99)
Applicant CAMILLERI, Patrick et al	

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

18 December 2000 (18.12.00)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer R. Chrem Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

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NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

GIDDINGS, Peter, John
SmithKline Beecham
Two New Horizons Court
Brentford
Middlesex TW8 9EP
ROYAUME-UNI

Date of mailing (day/month/year) 16 February 2001 (16.02.01)		IMPORTANT NOTIFICATION International filing date (day/month/year) 16 June 2000 (16.06.00)	
Applicant's or agent's file reference ML/P32328			
International application No. PCT/GB00/02364			
1. The following indications appeared on record concerning: <input checked="" type="checkbox"/> the applicant <input checked="" type="checkbox"/> the inventor <input type="checkbox"/> the agent <input type="checkbox"/> the common representative			
Name and Address GUÉDAT, Philippe University of Cambridge Department of Chemistry University Chemical Laboratory Lensfield Road Cambridge CB2 1EW United Kingdom		State of Nationality FR	State of Residence FR
		Telephone No.	
		Facsimile No.	
		Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning: <input type="checkbox"/> the person <input type="checkbox"/> the name <input checked="" type="checkbox"/> the address <input type="checkbox"/> the nationality <input checked="" type="checkbox"/> the residence			
Name and Address GUÉDAT, Philippe Lipha S.A. France Centre de Recherche et Développement de Lyon 115 Avenue Lacassagne F-69424 Lyon Cedex 03 France		State of Nationality FR	State of Residence FR
		Telephone No.	
		Facsimile No.	
		Teleprinter No.	
3. Further observations, if necessary:			
4. A copy of this notification has been sent to: <input checked="" type="checkbox"/> the receiving Office <input type="checkbox"/> the designated Offices concerned <input type="checkbox"/> the International Searching Authority <input checked="" type="checkbox"/> the elected Offices concerned <input checked="" type="checkbox"/> the International Preliminary Examining Authority <input type="checkbox"/> other:			
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35		Authorized officer R. Chrem Telephone No.: (41-22) 338.83.38	


PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference ML/P32328		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB00/02364	International filing date (day/month/year) 16/06/2000	Priority date (day/month/year) 16/06/1999
International Patent Classification (IPC) or national classification and IPC C07K7/00		
Applicant SMITHKLINE BEECHAM P.L.C.		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input checked="" type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application 		
Date of submission of the demand 18/12/2000		Date of completion of this report 23.03.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Lopez Garcia, F Telephone No. +49 89 2399 2171



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02364

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:

Description, pages:

1-18 as originally filed

Claims, No.:

1-33 as originally filed

Drawings, sheets:

1/5-5/5 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02364

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-33(yes)
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-33(yes)
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-33(yes)
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB00/02364

R Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 19-32 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

D1: WO 99 29712 A

D2: WO 00 27795 A

D3: R.S. WEEKS ET AL PROCEEDINGS OF THE 1999 AACR-NCI-EORTC INTERNATIONAL CONFERENCE ON MOLECULAR TARGETS AND CANCER THERAPEUTICS, vol. 5, no. Abs. 189, November 1999.

D4: G BYK ETAL J. MED. CHEM. vol. 41, 1998, p. 224-235.

D5: WO 97 18185 A

D6: US-A-5 767 099

D7: WO 97 03939 A

D8: WO 98 40502 A

D9: US-A-5 744 335

2. Present subject-matter appears to be supported by the priority document and documents D1-D3 are therefore not taken into account for present preliminary examination.
3. Documents D4-D9 describe spermine derivatives and analogs which enhance transfection but none of them fall within the scope of claim 1-18. Therefore, the subject-matter of claims 1-33 is novel (Art. 33(2) PCT).

4. In light of the prior art of D4-D9, the technical problem to be solved can be regarded as the provision of alternative transfection agents.

The problem is solved by the present application by the provision of compounds of claims 1-10, 13-16 and 18, which differ from the compounds of the art by the simultaneous presence of two hydrocarbyl and two amino acid groups bound to the N groups of spermine. There are in the art no indications that would suggest this specific compound template to the skilled person when faced with the problem of providing alternative transfection agents. Therefore, the subject-matter of claims 1-10, 13-16 and 18 is also considered as inventive (Art. 33(3) PCT).

The use and the preparation of these compounds are considered as inventive (Art. 33(3) PCT).

Compounds of claims 11, 12 and 17 are considered inventive due to their contribution to process for the preparation of compounds of claim 1 (Art. 33(3) PCT).

5. For the assessment of the present claims 19-32 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VII

Certain defects in the international application

1. The vague and imprecise statement in the description "without limitation" on p. 5, l. 10 implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity of the claims (Article 6 PCT) when used to interpret them (see the PCT Guidelines, C-III, 4.3a).
2. The terms PLUS employed in claim 22 and appearing to be a registered trade

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB00/02364

mark has no precise meaning as it is not internationally accepted as a standard descriptive term, thereby rendering the definition of the subject-matter of this claims 22 unclear (Article 6 PCT).

3. It is unclear whether the Applicant intends the expression used in brackets in claim 29 to be limiting or not. This renders the subject-matter of said claim unclear (Art. 6 PCT).
4. Term "hydrocarbyl" only embraces groups only having carbon and hydrogen atoms. Therefore, radical of claim 10 do not fall within this definition. This renders to subject-matter of claims 1 and 10 unclear (Art. 6 PCT).

Re Item VIII

Certain observations on the international application

1. The scope of claim 19 is extended in a vague and ambiguous manner by the term "analog", rendering it difficult for the skilled person to reduce the invention to practice without undue experimental effort. Therefore, the subject-matter of claim 19 does not fulfil the requirements of Art. 6 PCT.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



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21 December 2000 (21.12.2000)

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(10) International Publication Number
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(22) International Filing Date: 16 June 2000 (16.06.2000)

(25) Filing Language: English

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(30) Priority Data:
9914045.1 16 June 1999 (16.06.1999) GB

(71) Applicants (for all designated States except US):
SMITHKLINE BEECHAM P.L.C. [GB/GB]; New
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(GB).

(81) Designated States (national): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE,
DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO,
NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM,
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patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— Without international search report and to be republished
upon receipt of that report.

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: NOVEL COMPOUNDS

(57) Abstract: Spermine:peptide-based surfactant compounds are disclosed. The compounds are based on a spermine backbone with peptide groups and optionally hydrocarbyl groups linked thereto. Uses of the spermine:peptide-based surfactant compounds and methods for their production are also disclosed.



WO 00/77032 A2

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
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WO 00/77032 A3

(51) International Patent Classification⁷: C07C 233/36,
237/10, C07D 209/48, C07K 5/06, 5/02, A61K 48/00,
C12N 15/87

Cambridgeshire CB2 1EW (GB). KREMER, Andreas
[DE/GB]; SmithKline Beecham Pharmaceuticals, New
Frontiers Science Park South, Third Avenue, Harlow,
Essex CM19 5AW (GB).

(21) International Application Number: PCT/GB00/02364

(22) International Filing Date: 16 June 2000 (16.06.2000)

(74) Agent: GIDDINGS, Peter, John; SmithKline Beecham,
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(GB).

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
9914045.1 16 June 1999 (16.06.1999) GB

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE,
DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO,
NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(71) Applicants (*for all designated States except US*):
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CAMBRIDGE UNIVERSITY TECHNICAL SER-
VICES LTD. [GB/GB]; The Old Schools, Cambridge
University, Cambridge, Cambridgeshire CB2 1TS (GB).

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): CAMILLERI,
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New Frontiers Science Park South, Third Avenue, Harlow,
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Published:

— With international search report.

(88) Date of publication of the international search report:
31 May 2001

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

WO 00/77032 A3

(54) Title: SPERMINE:PEPTIDE-BASED SURFACTANT COMPOUNDS

(57) Abstract: Spermine:peptide-based surfactant compounds are disclosed. The compounds are based on a spermine backbone with peptide groups and optionally hydrocarbyl groups linked thereto. Uses of the spermine:peptide-based surfactant compounds and methods for their production are also disclosed.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/02364

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C233/36 C07C237/10 C07D209/48 C07K5/06 C07K5/02
A61K48/00 C12N15/87

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C07C C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data, BIOSIS, MEDLINE, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 99 29712 A (CAMILLERI PATRICK ;RICE SIMON QUENTYN JOHN (GB); KREMER ANDREAS (G) 17 June 1999 (1999-06-17) the whole document	1,19-33
P,X	WO 00 27795 A (LIFE TECHNOLOGIES INC) 18 May 2000 (2000-05-18) abstract; claims	1,19-33
	-/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

23 November 2000

Date of mailing of the international search report

07/12/2000

Name and mailing address of the ISA

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Authorized officer

Cervigni, S

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/02364

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	R.S. WEEKS ET AL: "Novel lysine-spermine conjugate alters in vivo and in vitro tumor cell growth through inhibition of polyamine transport" PROCEEDINGS OF THE 1999 AACR-NCI-EORTC INTERNATIONAL CONFERENCE ON MOLECULAR TARGETS AND CANCER THERAPEUTICS, 'Online! vol. 5, no. Abs. 189, November 1999 (1999-11), XP002153599 Retrieved from the Internet: <URL:http://aacr.edoc.com/newdrugs/189.htm 1> 'retrieved on 2000-11-22! abstract	1,19-33
A	G BYK ETAL: "Synthesis, activity and structure-activity relationship studies of novel cationic lipids for DNA transfer" JOURNAL OF MEDICINAL CHEMISTRY,US,AMERICAN CHEMICAL SOCIETY. WASHINGTON, vol. 41, no. 2, 15 January 1998 (1998-01-15), pages 224-235, XP002118261 ISSN: 0022-2623	
A	WO 97 18185 A (DUBERTRET CATHERINE ;SCHWARTZ BERTRAND (FR); BYK GERARDO (FR); SCH) 22 May 1997 (1997-05-22)	
A	US 5 767 099 A (HUBBARD SHIRLEY C ET AL) 16 June 1998 (1998-06-16)	
A	WO 97 03939 A (DWYER BRIAN PATRICK ;GENTA INC (US); BROWN BOB DALE (US); DAILY WI) 6 February 1997 (1997-02-06)	
A	WO 98 40502 A (LIFE TECHNOLOGIES INC) 17 September 1998 (1998-09-17)	
A	US 5 744 335 A (FRITZ JEFFERY ET AL) 28 April 1998 (1998-04-28)	

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter. Appl. Application No

PCT/GB 00/02364

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9929712 A	17-06-1999	EP 1037903 A	27-09-2000
WO 0027795 A	18-05-2000	AU 1477600 A	29-05-2000
WO 9718185 A	22-05-1997	FR 2741066 A	16-05-1997
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		JP 10510813 T	20-10-1998
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		NZ 313839 A	23-12-1998
WO 9840502 A	17-09-1998	US 6051429 A	18-04-2000
		AU 6562298 A	29-09-1998
		EP 1007699 A	14-06-2000
US 5744335 A	28-04-1998	NONE	